Effective Adaptive Immunity Relies on Lymph Node Remodeling

PI(s) of MSM U01: David C. Zawieja and James E. Moore Jr.

Institution(s): Texas A&M University and Imperial College London

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Abstract Authors

Sarah Johnson, Lowell Edgar, Daniel Watson, David Zawieja and James Moore Jr.

Abstract Text

Adaptive immunity relies on a combination of biological and physical actions being carefully coordinated inside lymph nodes. Antigen-presenting cells (APCs) arriving in afferent lymph are distributed around the periphery of the node in the subcapsular sinus, and then are directed into the porous medium structure of the cortex by gradients in chemokine concentrations. Chemokines are produced by resident lymph node cells, and rely on a combination of diffusion, advection, extracellular matrix binding, and cell-mediated modifications to establish and maintain concentration gradients. The APCs must then communicate effectively with T cells in sufficient numbers that the appropriate distribution of T cell subtypes is achieved. A commonly observed characteristic of this adaptation process is lymph node swelling, in which the node might grow to several times its baseline volume.

Context: We have developed a hybrid Agent-Based Model (ABM) – Transport model to provide a better understanding of adaptive immunity. Node swelling was varied as an input parameter of maximum volume change allowed.

Data: Following the initiation of a stimulus intended to simulate an incoming antigen or vaccination (total duration of four days), T cell numbers increased within hours, peaked at 2.5X on day 3, and remained elevated for 10 days. T cell activation peaked at day 2, and was sustained through day 6. Allowing the node to expand up to 2.8X its baseline volume resulted in proportionally greater numbers of activated T cells. The number of effector T cells was reduced at higher maximum volumes, but this result was not robust to parameter variation analysis. These results indicate a potentially important role for lymph node swelling as a means for allowing not only for increased T cell numbers, but also enhanced T cell activation and subsequent differentiation.

Evaluation: Under baseline conditions, the dynamics of experimentally observed random walk-like behavior of T cells were reproduced. The time courses of T cell expansion and differentiation corresponded well with experimental results that were not used in the construction of the model.

Limitations: Experimental data on cell interactions are available in the literature, but the effects of limiting or increasing lymph node expansion are not well studied.

Version control: Source code and text input files are maintained in lab repositories. To avoid confusion, only the final version of the code will be made available publicly.

Documentation: The development of comprehensive model documentation is ongoing.

Dissemination: Current prototype models are not yet in a state suitable for broad dissemination.

Independent reviews: The results from these models will soon be submitted for publication.

Test competing implementations: We are not aware of competing models, but remain ready and enthusiastic about expanding the capabilities of our models through collaboration.

Conform to standards: We use standard coding practices, and have implemented our models in RepastSymphony as well as PYTHON.